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(FILE 'HOME' ENTERED AT 13:57:37 ON 17 APR 2006)

FILE 'REGISTRY' ENTERED AT 13:58:05 ON 17 APR 2006
L1 SCREEN 2076
L2 STRUCTURE UPLOADED
L3 QUE L2 AND L1
L4 1 S L3 FUL

FILE 'CAPLUS' ENTERED AT 13:59:21 ON 17 APR 2006
L5 10 S L4/THU
L6 0 S DYSLIPOPROTEINEMIA/AI
L7 401 S DYSLIPOPROTEINEMIA/IA
L8 0 S L5 AND L7
L9 43 S L4
L10 0 S L9 AND L7
L11 162189 S CHOLESTEROL/IA
L12 14 S L11 AND L9

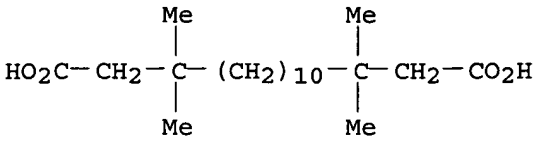
L12 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:611928 CAPLUS
DOCUMENT NUMBER: 143:91061
TITLE: Methods of administering 3,3,14,14 tetramethyl hexadecane 1,16 dioic acid
INVENTOR(S): Bar-Tana, Jacob; Bekersky, Ihor
PATENT ASSIGNEE(S): Syndrome X Ltd., Israel
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005062718	A2	20050714	WO 2004-IL1185	20041230
WO 2005062718	A3	20051110		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-533639P P 20031230
AB The present invention provides methods for lowering LDL, VLDL, total **cholesterol**, triglycerides, insulin resistance and hypertension, and methods for elevating HDL in subjects in need thereof. Addnl., the present invention provides methods of administering 3,3,14,14 tetra-Me hexadecane 1,16 dioic acid for the above indications.
IT **87272-20-6**, Medica 16
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of administering 3,3,14,14 tetra-Me hexadecane 1,16 dioic acid)
RN 87272-20-6 CAPLUS

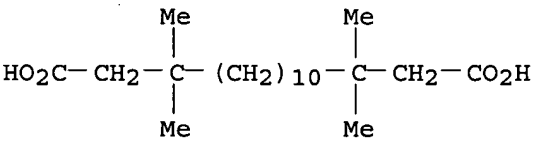
CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)



L12 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:80358 CAPLUS
DOCUMENT NUMBER: 140:139513
TITLE: Methods of identifying compounds that affect a fatty acid cell-surface receptor
INVENTOR(S): Owman, Christer; Olde, Bjorn; Kotarsky, Knut; Nilsson, Niclas; Flodgren, Erik
PATENT ASSIGNEE(S): Swed.
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004019109	A1	20040129	US 2002-202687	20020724
PRIORITY APPLN. INFO.:			US 2002-202687	20020724

AB The present invention provides methods for screening and identifying compds. that affect the metabolism of fatty acids and fatty acid derivs., and thus for compds. that possess anti-diabetic as well as anti-obesity properties and possess the ability to affect the levels of chylomicrons, triacylglycerols, cholesterols, and fatty acids in a patient. Kits and compns. for screening and identifying such compds. are also provided. The invention is predicated on the identification of a physiol. receptor for free fatty acids and anti-diabetic and anti-obesity drugs.
IT **87272-20-6**, MEDICA 16
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(methods of identifying compds. that affect a fatty acid cell-surface receptor)
RN 87272-20-6 CAPLUS
CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)



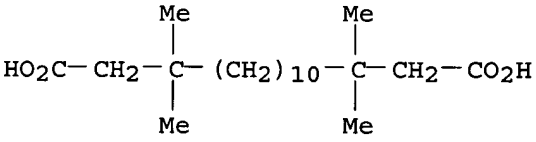
L12 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:775950 CAPLUS
DOCUMENT NUMBER: 128:71008
TITLE: Sensitization to insulin induced by β,β'-methyl-substituted hexadecanedioic acid (MEDICA 16) in obese Zucker rats in vivo
AUTHOR(S): Mayorek, Nina; Kalderon, Bella; Itach, Etty; Bar-Tana, Jacob

CORPORATE SOURCE: Department of Human Nutrition and Metabolism, Faculty of Medicine, The Hebrew University, Jerusalem, 91120, Israel
SOURCE: Diabetes (1997), 46(12), 1958-1964
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB β,β'-Methyl-substituted hexadecanedioic acid (MEDICA 16) consists of a nonmetabolizable long-chain fatty acid designed to probe the effect exerted by fatty acids on insulin sensitivity. The effect of MEDICA 16 was evaluated in insulin-resistant Zucker (fa/fa) rats in terms of liver, muscle, and adipose tissue response to clamped euglycemic hyperinsulinemia in vivo. Nontreated Zucker rats were insulin resistant, maintaining basal rates of total-body glucose disposal, glucose production in liver, free fatty acid (FFA) flux into plasma, and FFA re-esterification in adipose tissue, irresp. of the insulin levels induced. MEDICA 16 treatment resulted in an insulin-induced decrease in hepatic glucose production, together with an insulin-induced increase in total-body glucose disposal. Intracellular re-esterification of lipolyzed FFA in adipose tissue was specifically activated by MEDICA 16, resulting in a pronounced decrease in FFA release, with a concomitant decrease in plasma FFA. In conclusion, MEDICA 16 treatment results in the sensitization of liver, muscle, and adipose tissue to insulin in an animal model for obesity-induced insulin resistance.

IT **87272-20-6**, MEDICA 16
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(MEDICA 16 fatty acid analog induction of sensitization of liver, muscle, and adipose tissue to insulin in animal model for obesity-induced insulin resistance)

RN 87272-20-6 CAPLUS
CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:743236 CAPLUS
DOCUMENT NUMBER: 123:160424

TITLE: Inhibition of atherosclerosis and myocardial lesions in the JCR:LA-cp rat by β,β'-tetramethylhexadecanedioic acid (MEDICA 16)

AUTHOR(S): Russell, James C.; Amy, Roger M.; Graham, Sandra E.; Dolphin, Peter J.; Wood, George O.; Bar-Tana, Jacob
CORPORATE SOURCE: Department of Surgery, University of Alberta, Edmonton, AB, T6G 2S2, Can.

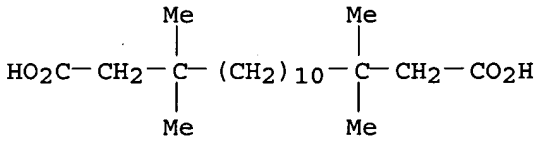
SOURCE: Arteriosclerosis, Thrombosis, and Vascular Biology (1995), 15(7), 918-23
CODEN: ATVBFA; ISSN: 1079-5642
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Atherosclerosis-prone, insulin-resistant JCR:LA-cp male rats were treated

from 6 wk to 39 wk of age with β,β'-tetramethylhexadecanedioic acid (MEDICA 16). Body wts. were reduced (13%) at 36 wk without any accompanying decrease in food consumption. The treatment did not cause any significant change in plasma glucose or fasting insulin concns. There was a significant decrease in the extreme hyperplasia of the islets of Langerhans (38%). The marked VLDL hypertriglyceridemia was decreased by 70%, with an accompanying significant reduction in **cholesterol** concns. The severity of raised atherosclerotic lesions on the aortic arch was very markedly reduced in treated rats. This was accompanied by a reduction in the incidence of ischemic myocardial lesions. The authors conclude that long-term (33 wk) MEDICA 16 treatment of an animal model for the obesity/insulin-resistant/hyperlipidemic syndrome not only markedly improved lipid metabolism, but also inhibited the development of advanced cardiovascular disease.

IT **87272-20-6**, MEDICA 16
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of atherosclerosis and myocardial ischemic lesions in JCR:LA-cp rat by methylhexadecanedioic acid (MEDICA 16))

RN 87272-20-6 CAPLUS
CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)



L12 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:208327 CAPLUS
DOCUMENT NUMBER: 120:208327
TITLE: The effect of β,β'-tetramethylhexadecanedioic acid (MEDICA 16) on plasma very-low-density lipoprotein metabolism in rats: role of apolipoprotein C-III
AUTHOR(S): Frenkel, Baruch; Bishara-Shieban, Janette; Bar-Tana, Jacob
CORPORATE SOURCE: Hadassah Fac. Med., Hebrew Univ., Jerusalem, 91010, Israel
SOURCE: Biochemical Journal (1994), 298(2), 409-14
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English

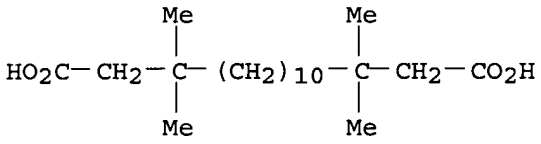
AB Short term treatment of rats with β,β'-tetramethylhexadecanedioic acid (MEDICA 16) results in a pronounced decrease in plasma very-low-d.-lipoprotein (VLDL) **cholesterol** and VLDL triacylglycerol, previously ascribed to a decrease in liver VLDL production (J. Bar-Tana et al, 1988). The hypolipidemic effect of MEDICA 16 was further analyzed here by monitoring plasma VLDL clearance and its hepatic uptake. VLDL triacylglycerol and VLDL apolipoprotein (apo) B fractional clearance rates were increased 7-8-fold in MEDICA 16-treated rats. The increase in the fractional clearance rate of plasma VLDL was essentially eliminated by functional hepatectomy. It was accounted for by activation of plasma VLDL uptake by the liver being completed during the first 4 min after the injection of the VLDL label and before commencement of uptake in non-treated animals. The hypolipidemic effect of MEDICA 16 was accompanied by a 3.5-fold decrease in plasma apoC-III, but plasma apoC-III clearance remained unaffected by MEDICA 16. MEDICA 16-induced premature hepatic uptake of plasma VLDL due to suppression of apoC-III

production may thus account for enhancement of plasma VLDL clearance in treated animals.

IT **87272-20-6**, MEDICA 16
RL: BIOL (Biological study)
(plasma very-low-d. lipoprotein metabolism response to, apolipoprotein C-III in)

RN 87272-20-6 CAPLUS

CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)



L12 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:183022 CAPLUS

DOCUMENT NUMBER: 120:183022

TITLE: Use of α,ω-dicarboxylic acids to lower fibrinogen levels

INVENTOR(S): Pill, Johannes; Doerge, Liesel; Stegmeier, Karlheinz

PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Germany

SOURCE: Ger. Offen., 6 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

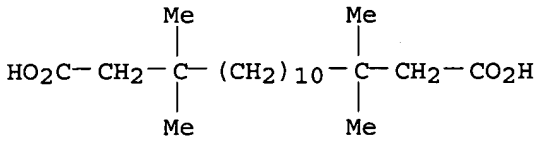
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4224670	A1	19940127	DE 1992-4224670	19920725
WO 9402128	A1	19940203	WO 1993-EP1894	19930717
W: AU, BG, BR, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RO, RU, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 652750	A1	19950517	EP 1993-915948	19930717
EP 652750	B1	19971217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 07509233	T2	19951012	JP 1994-504141	19930717
JP 3633614	B2	20050330		
HU 70510	A2	19951030	HU 1995-217	19930717
AU 684465	B2	19971218	AU 1993-45702	19930717
AU 9345702	A1	19940214		
AT 161176	E	19980115	AT 1993-915948	19930717
IL 106455	A1	19970814	IL 1993-106455	19930722
ZA 9305331	A	19950123	ZA 1993-5331	19930723
NO 9500255	A	19950124	NO 1995-255	19950124
US 5641810	A	19970624	US 1995-373264	19950125
PRIORITY APPLN. INFO.:			DE 1992-4224670 A	19920725
			WO 1993-EP1894 W	19930717

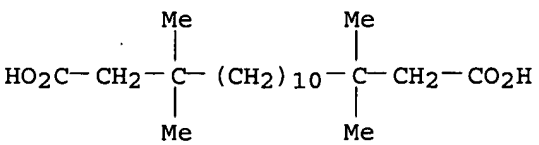
AB The title compds., (HO2CCXYCR1R2)2Q [X, Y = H, halo, OH, cyano, CO2H, C1-6 alkyl or alkoxy or alkoxycarbonyl, carbamoyl; R1, R2 = H, C1-6 alkyl; Q = C2-14 (un)saturated alkylene in which ≥1 C atom may be replaced with a cyclohexane, benzene, or heterocyclic ring] (I) and their in vivo hydrolyzable carboxy derivs. are useful for lowering blood fibrinogen levels to treat or prevent obstructive vascular disorders resulting from hyperfibrinogenemia. Thus, the turpentine-induced elevation in plasma fibrinogen in rats was prevented by prior treatment with I [X = Y = Cl, R1 = R2 = H, Q = (CH2)8] (25 mg/kg/day orally in 1% tylose suspension).

IT **87272-20-6**

RL: BIOL (Biological study)
(fibrinogen of blood lowering with)
RN 87272-20-6 CAPLUS
CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)



L12 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:116529 CAPLUS
DOCUMENT NUMBER: 118:116529
TITLE: Hypocholesterolemic effect of ββ'-methyl-substituted hexadecanedioic acid (MEDICA 16) in the male hamster
AUTHOR(S): Mayorek, Nina; Bar-Tana, Jacob
CORPORATE SOURCE: Hadassah Med. Sch., Hebrew Univ., Jerusalem, 91010, Israel
SOURCE: Biochemical Journal (1993), 289(3), 911-17
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Treatment of **cholesterol**-fed male hamsters kept on a diet of purina chow with ββ'-methyl-substituted hexadecanedioic aci (MEDICA 16) resulted in a progressive hypocholesterolemic effect, amounting to a 50% decrease in the **cholesterol** content of all plasma lipoproteins. The decrease in plasma **cholesterol** could be accounted for by activation of plasma-**cholesterol** efflux through the liver into the bile mediated by MEDICA 16-induced (a) increase of the number of liver LDL receptors, (b) activation of liver neutral cholesteryl ester hydrolase with a concomitant inhibition of liver acyl-CoA **cholesterol** acyltransferase, resulting in shifting of the liver cholesteryl ester/free-**cholesterol** cycle in the direction of free **cholesterol**, and (c) activation of **cholesterol** efflux from the liver into the bile. The increase in bile **cholesterol** output was accompanied by an increase in bile phospholipids but not in bile acids. In contrast with rats, MEDICA 16-treatment of male hamsters did not result in a hypotriacylglycerolemic effect, inhibition of lipogenesis, nor in a substantial decrease in plasma apolipoprotein C-III content.
IT **87272-20-6**, MEDICA 16
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(hypocholesterolemic activity of, mechanism of)
RN 87272-20-6 CAPLUS
CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)

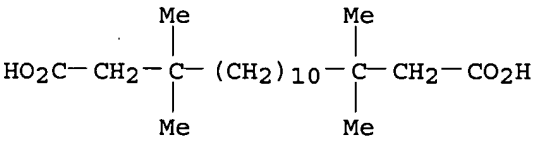


L12 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:590844 CAPLUS

DOCUMENT NUMBER: 117:190844
TITLE: Effect of β,β'-tetramethyl-substituted hexadecanedioic acid (MEDICA 16) on laying hen performance and egg yolk lipid composition
AUTHOR(S): Elkin, R. G.; Rogler, J. C.; Lee, H. D.; Watkins, B. A.
CORPORATE SOURCE: Dep. Anim. Sci., Purdue Univ., West Lafayette, IN, 47907, USA
SOURCE: British Poultry Science (1992), 33(3), 677-81
CODEN: BPOSA4; ISSN: 0007-1668
DOCUMENT TYPE: Journal
LANGUAGE: English

AB β,β'-Tetramethyl-substituted hexadecanedioic acid (MEDICA 16), an inhibitor of hepatic cholesterogenesis and lipogenesis in rats, was orally administered to 24-wk-old White Leghorn hens for a period of 16 days. Hens were fed maize-soybean meal diets containing 0, 1.5, or 3.0 g MEDICA 16/kg. Although MEDICA 16 did not affect egg weight, yolk weight, egg **cholesterol** content, or the efficiency of food utilization, egg production was significantly reduced in birds fed 3.0 g MEDICA 16/kg compared to those fed the other two diets. Total yolk monounsatd. fatty acids were significantly higher in eggs of hens fed both inclusion rates of MEDICA 16 compared to those of the control birds. In contrast, egg yolk total polyunsatd. fatty acid content and the ratio of polyunsatd. to saturated fatty acids were both inversely related to the dietary content of MEDICA 16. These results suggest that MEDICA 16 primarily altered hepatic fatty acid metabolism, but not **cholesterol** synthesis, in laying hens.

IT **87272-20-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(feeding experiment with, on laying hens, egg production and yolk lipid composition
in relation to)
RN 87272-20-6 CAPLUS
CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)



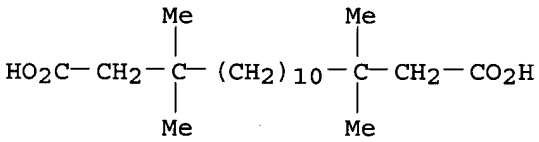
L12 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:441637 CAPLUS
DOCUMENT NUMBER: 115:41637
TITLE: Hypolipidemic effect of β,β'-tetramethylhexadecanedioic acid (MEDICA 16) in hyperlipidemic JCR:LA-corpulent rats
AUTHOR(S): Russell, James C.; Dolphin, Peter J.; Hameed, Morad; Stewart, Bruce; Koeslag, Dorothy G.; Rose-Kahn, Gene; Bar-Tana, Jacob
CORPORATE SOURCE: Dep. Surg., Univ. Alberta, Edmonton, AB, T6G 2S2, Can.
SOURCE: Arteriosclerosis and Thrombosis (1991), 11(3), 602-9
CODEN: ARTTE5; ISSN: 1049-8834
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Short-term treatment of male and female obese JCR:LA-corpulent rats with β,β'-tetramethylhexadecanedioic acid (MEDICA 16) resulted in a marked decrease (as much as 80%) in plasma triglyceride values, with a concomitant decrease in the highly elevated very low d. lipoprotein (VLDL) levels of the corpulent rat. There were modest decreases in

cholesterol levels and increases in low d. lipoprotein and high d. lipoprotein lipids. The concns. of apolipoproteins C-II and C-III were decreased in both the whole-serum and the VLDL fractions. Food consumption, rate of weight gain, fasting insulin levels, and the integrated insulin response to an i.v. glucose load remained unaffected. The decrease in plasma VLDL may be accounted for by inhibition of liver long-chain fatty acid synthesis at the level of ATP citrate lyase, with a concomitant reduction of VLDL triglyceride production by the liver. This decrease in plasma VLDL production was accompanied by a two-fold to three-fold increase in the triglyceride and **cholesterol** components of the low d. lipoprotein and high d. lipoprotein fractions, together with a two-fold to four-fold decrease in plasma apolipoprotein, indicating that activation of plasma VLDL catabolism may further account for the overall hypolipidemic effect induced by MeDICA 16. The overall hypolipidemic effect of MEDICA 16 may be expected to inhibit the spontaneous atherogenic sequelae induced in the corpulent rat by severe VLDL hyperlipidemia.

IT **87272-20-6**, MEDICA 16
RL: PRP (Properties)
(hypolipidemic effect of, in obesity and hyperlipidemia, atherosclerosis in relation to)

RN 87272-20-6 CAPLUS
CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)



L12 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:33587 CAPLUS
DOCUMENT NUMBER: 110:33587
TITLE: Hypolipidemic, antiobesity, and hypoglycemic-hypoinsulinemic effects of β,β'-methyl-substituted hexadecanedioic acid in sand rats
AUTHOR(S): Tzur, Ruth; Rose-Kahn, Gene; Adler, Jonathan H.; Bar-Tana, Jacob
CORPORATE SOURCE: Hadassah Med. Sch., Hebrew Univ., Jerusalem, Israel
SOURCE: Diabetes (1988), 37(12), 1618-24
CODEN: DIAEAZ; ISSN: 0012-1797
DOCUMENT TYPE: Journal
LANGUAGE: English

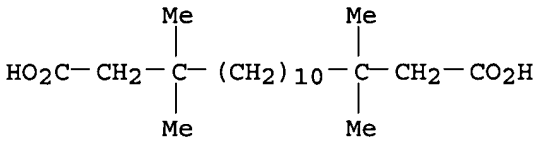
AB Treatment of sand rats kept on a balanced lab chow diet ad libitum with β,β'-tetramethyl-substituted hexadecanedioic acid (MEDICA 16) resulted in a hypolipidemic effect accompanied by an extensive reduction in adiposity, with a concomitant hypoglycemic-hypoinsulinemic effect. The overall effect was sustained as long as the drug was administered. The hypolipidemic effect of MEDICA 16 consisted of a 70 and 40% decrease in plasma triacylglycerols and **cholesterol**, resp., and resulted from inhibition of liver lipogenesis and cholesterogenesis. Adipose reduction by MEDICA 16 treatment or calorie restriction consisted of a 75-90% decrease in the perirenal, omental, epididymal, and s.c. fat, with a 50% decrease in liver neutral lipids. The reduction in adiposity was accounted for by a resp. decrease in the lipid content of individual adipocytes, with a concomitant decrease in the number of adipocytes of selected adipose tissues. The decrease induced in adiposity by MEDIA 16 treatment could not be accounted for by anorectic or cathartic effects of the drug. The hypoglycemic-hypoinsulinemic effect of MEDICA 16 consisted of amelioration of the tolerance of glucose with normalization of plasma insulin. It was

accompanied by 8-fold increase in the number of insulin receptors in epididymal adipocytes, which was, however, counteracted by a decrease in their affinity for insulin. The receptor and postreceptor effects exerted by MEDICA 16 were similar to those of calorie restriction. The overall effect of MEDICA 16 in rats may reflect the pharmacol. potential of MEDICA compds. in pathol. hyperlipidemic-obesity-diabetic syndromes.

IT **87272-20-6**, MEDICA 16
RL: BIOL (Biological study)
(hyperlipidemia-obesity-diabetes mellitus syndrome treatment with)

RN 87272-20-6 CAPLUS

CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)



L12 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:473019 CAPLUS

DOCUMENT NUMBER: 109:73019

TITLE: Preparation of long-chain α,ω-dicarboxylic acids and derivatives and pharmaceutical compositions containing them useful in reducing serum **cholesterol** and triglyceride levels

INVENTOR(S): Bar-Tana, Jacob

PATENT ASSIGNEE(S): Epis S. A., Switz.

SOURCE: U.S., 20 pp. Cont.-in-part of U.S. Ser. No. 443,315, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 4689344	A	19870825	US 1984-623673		19840622
US 4634795	A	19870106	US 1985-769765		19850827
PRIORITY APPLN. INFO.:			IL 1981-64542	A	19811215
			US 1982-443315	A2	19821122

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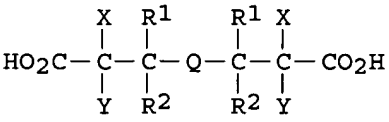


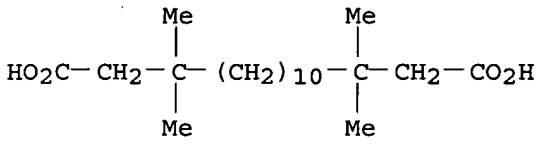
I

AB Title acids I [R1, R2 = (un)substituted hydrocarbyl, heterocyclyl; X, Y, = H, halo, cyano, CO2H, alkoxycarbonyl, carbamoyl, (un)substituted alkyl; one of X and Y may = alkoxy, OH, or cyano; Q = linear C8-14 chain optionally containing heteroatoms, inert substituents, or a ring] and their derivs. are prepared as anticholesterolemics and hypolipidemics. Grignard reaction of Br(CH2)10Br with Me2C:C(CO2Et)2 in THF containing Cu2Cl2 gave (EtO2C)2CHCMe2(CH2)10CMeCH(CO2Et)2, which underwent saponification in refluxing aqueous 25% KOH with decarboxylation of the resultant tetracarboxylic acid at 150-160° to give HO2CCH2CMe2(CH2)10CMe2CH2CO2H (II). At 250

mg/kg/day orally in rats, II gave 80% inhibition of hepatic neutral fat synthesis as determined by 3H2O incorporation.

IT **87272-20-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as anticholesterolemic)

RN 87272-20-6 CAPLUS
CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)

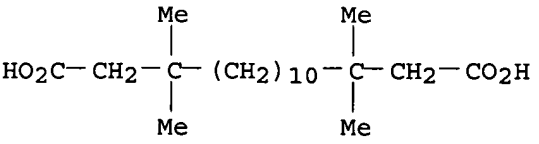


L12 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:448226 CAPLUS
DOCUMENT NUMBER: 109:48226
TITLE: Hypolipidemic effect of β,β'-methyl-substituted hexadecanedioic acid (MEDICA 16) in normal and nephrotic rats
AUTHOR(S): Bar-Tana, Jacob; Rose-Kahn, Gene; Frenkel, Baruch; Shafer, Zehava; Fainaru, Menachem
CORPORATE SOURCE: Dep. Biochem., Jerusalem, 91010, Israel
SOURCE: Journal of Lipid Research (1988), 29(4), 431-41
CODEN: JLPRAW; ISSN: 0022-2275
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Treatment of normal or puromycin aminonucleoside-nephrotic rats, kept on a balanced diet, with β,β'-tetramethyl-substituted hexadecanedioic acid (MEDICA 16) resulted in an acute reversible inhibition of liver lipogenesis and cholesterogenesis with a concomitant hypolipidemic effect, which was sustained as long as the drug was administered. The hypolipidemic effect in normal and nephrotic rats consisted of 70-80% and 40-60% reduction, resp., in plasma very-low-d. lipoprotein (VLDL)-triacylglycerols and **cholesterol**, with a resp. increase in the high-d. lipoprotein **cholesterol**/(VLDL plus LDL)-**cholesterol** ratio. The observed hypolipidemic effect was accompanied by a 10-fold decrease in VLDL-apoC-III content with a concomitant enrichment of the VLDL fraction by VLDL remnants having an increased apoB-100/apoB-48 ratio. The pharmacol. reduction of VLDL by MEDICA 16 may offer a treatment mode of choice for selected hyperlipidemic states.

IT **87272-20-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(hypolipidemic activity of, in normal and nephrotic animals)

RN 87272-20-6 CAPLUS
CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)

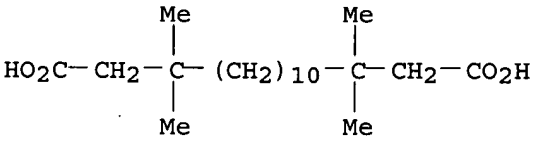


L12 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:416874 CAPLUS
DOCUMENT NUMBER: 109:16874

TITLE: The hypochylomicronemic effect of β,β'-methyl-substituted hexadecanedioic acid (MEDICA 16) is mediated by a decrease in apolipoprotein C-III
AUTHOR(S): Frenkel, Baruch; Mayorek, Nina; Hertz, Rachel; Bar-Tana, Jacob
CORPORATE SOURCE: Hadassah Med. Sch., Hebrew Univ., Jerusalem, 91010, Israel
SOURCE: Journal of Biological Chemistry (1988), 263(17), 8491-7
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Treatment of rats fed a balanced Purina Chow diet with β,β'-tetramethyl-substituted hexadecanedioic acid (MEDICA 16) resulted in an acute 70-80% decrease in plasma chylomicrons-triacylglycerols which was sustained as long as the drug was administered. The hypochylomicronemic effect resulted from an enhanced plasma clearance of chylomicrons whereas their intestinal production and absorption remained unaffected. The increased fractional clearance rate of plasma chylomicrons in MEDICA 16-treated rats presumably reflects the primary action of the drug rather than being secondary to the hypochylomicronemic state, since it was similarly observed in MEDICA 16-treated animals made transiently normolipidemic by loading them with intestinal lipid. The increase in the fractional clearance rate of plasma chylomicrons resulted from their enhanced uptake by the liver complemented with their activated extrahepatic catabolism. The activation of both catabolic modes in MEDICA 16-treated rats could be accounted for by a 10-fold decrease in the apo-C-III content of plasma chylomicrons. No increase was observed in hepatic apo-B,E or apo-E receptors, nor in the maximal capacity of lipoprotein lipase. The pharmacol. reduction of plasma apo-C-III may thus offer a treatment mode of choice for selected hyperlipidemic states.

IT **87272-20-6**
RL: PRP (Properties)
(hypochylomicronemic effect of, apolipoprotein C-III decrease mediation of)
RN 87272-20-6 CAPLUS
CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)



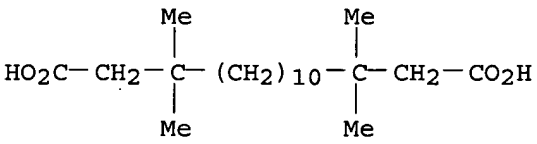
L12 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:516064 CAPLUS
DOCUMENT NUMBER: 103:116064
TITLE: Inhibition of lipid synthesis by ββ'-tetramethyl-substituted, C14-C22, α,ω-dicarboxylic acids in the rat in vivo
AUTHOR(S): Bar-Tana, Jacob; Rose-Kahn, Gene; Srebnik, Morris
CORPORATE SOURCE: Hadassah Med. Sch., Hebrew Univ., Jerusalem, 91010, Israel
SOURCE: Journal of Biological Chemistry (1985), 260(14), 8404-10
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB ββ'-Methyl-substituted α,ω-dicarboxylic acids (MEDICA) of C14-C18 chain length inhibited liver lipid synthesis in the

rat in vivo. Maximum inhibition was observed with MEDICA 16 [**87272-20-6**] amounting to a 50% decrease in fatty acid and **cholesterol** biosynthesis in the presence of 0.07 and 0.0156% (weight/weight) of the drug in the diet, resp. Inhibition of lipid biosynthesis by MEDICA 16 involved a reduction in cytosolic acetyl-CoA [72-89-9] content, whereas the C flux from glucose to glycogen, protein, and CO2 remained unaffected. Inhibition of lipogenesis by MEDICA 16 resulted in a 50% decrease in liver and carcass (but not brain) neutral lipid ester content at 0.25% (weight/weight) of the drug in the diet, as well as in a dose-dependent hypotriglyceridemic effect, with an up to 3-fold reduction in serum triacylglycerols. Inhibition of cholesterogenesis by MEDICA 16 resulted in a hypocholesterolemic effect, with 60 and 45% redns. in (very low d. plus low d. lipoprotein) **cholesterol** and high d. lipoprotein **cholesterol**, resp.

IT **87272-20-6**
RL: BIOL (Biological study)
(lipogenesis inhibition by)

RN 87272-20-6 CAPLUS
CN Hexadecanedioic acid, 3,3,14,14-tetramethyl- (9CI) (CA INDEX NAME)



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